***DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO 38° Ciclo***

**Titolo della ricerca:**

**Involvement of Multidrug efflux pumps in the virulence of pathogenic *E. coli***

**Docente guida proposto:**

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**DESCRIZIONE DELLA RICERCA**

Efflux pumps represent an important group of transporters found in all organisms. Their importance resides in their ability to extrude a wide range of antibiotics resulting in the emergence of multidrug resistance (MDR) in many bacteria (Du et al., 2018). Besides antibiotics, MDR efflux pumps are capable of excreting a large range of toxic substances including endogenous metabolites, thus facilitating the survival of bacteria under different environmental conditions (Alcade-Rico et al., 2016, Henderson et al., 2021, Pasqua et al., 2021)

This study is part of a larger project aimed at understanding the factors that contribute to virulence in pathogenic *E. coli* strains. Indeed, the pathogenicity of a bacterium is a multifactorial process in which several proteins are involved in the different stages of the pathogen's interaction with host target cells. In addition, the bacterium is able to sense the host environment and to trigger a response involving the coordinated activation of virulence genes. In this context, the regulation of many MDR efflux pumps by global regulatory networks, as the Two-Component Systems (TCS), reflects the need of the bacterial cell to fine tune the expression of MDR efflux pumps in response to a specific niche and in coordination with other virulence factors.

**Obiettivi della ricerca**

The aim of this research is to investigate on the functional role of some of the major MDR efflux pumps during the pathogenicity process of enteroaggregative E. coli (EAEC), a group of enteropathogenic *E. coli* strongly involved in gastrointestinal infections.

**Pertinent publications of the proponent (last 5 years)**

1: Skovajsová E, Colonna B, Prosseda G, Sellin ME, Di Martino ML. 2022. The

VirF21:VirF30 protein ratio is affected by temperature and impacts *Shigella*

*flexneri* host cell invasion. FEMS Microbiol Lett. 6:fnac043.

2: Pasqua M, Bonaccorsi di Patti MC, Fanelli G, Utsumi R, Eguchi Y, Trirocco R,

Prosseda G, Grossi M, Colonna B. 2021. Host - Bacterial Pathogen Communication: The

Wily Role of the Multidrug Efflux Pumps of the MFS Family. Front Mol Biosci.

8:723274.

3: Pasqua M, Zennaro A, Trirocco R, Fanelli G, Micheli G, Grossi M, Colonna B,

Prosseda G. 2021 Modulation of OMV Production by the Lysis Module of the DLP12

Defective Prophage of *Escherichia coli* K12. Microorganisms. 9:369.

4: Fanelli G, Pasqua M, Colonna B, Prosseda G, Grossi M. Expression Profile of

Multidrug Resistance Efflux Pumps During Intracellular Life of Adherent-Invasive

*Escherichia coli* Strain LF82. Front Microbiol. 2020 11:1935.

5: Pasqua M, Grossi M, Zennaro A, Fanelli G, Micheli G, Barras F, Colonna B,

Prosseda G. 2019 The Varied Role of Efflux Pumps of the MFS Family in the Interplay

of Bacteria with Animal and Plant Cells. Microorganisms. 7:285.

6: Pasqua M, Grossi M, Scinicariello S, Aussel L, Barras F, Colonna B, Prosseda

G. 2019 The MFS efflux pump EmrKY contributes to the survival of *Shigella* within

macrophages. Sci Rep. 9(1):2906.

7: Pasqua M, Michelacci V, Di Martino ML, Tozzoli R, Grossi M, Colonna B,

Morabito S, Prosseda G. 2017 The intriguing evolutionary journey of enteroinvasive

*E. coli* (EIEC) toward Pathogenicity. Front Microbiol. 8:2390.

8: Leuzzi A, Grossi M, Di Martino ML, Pasqua M, Micheli G, Colonna B, Prosseda

G. 2017 Role of the SRRz/Rz lambdoid lysis cassette in the pathoadaptive

evolution of *Shigella*. Int J Med Microbiol.307(4-5):268-275.

**References (other citations, if appropriate)**

Alcalde-Rico, M.; Hernando-Amado, S.; Blanco, P.; Martínez, J.L. **2016** Multidrug efflux pumps at the crossroad between antibiotic resistance and bacterial virulence. *Front. Microbiol.*, *7*, 1483.

Du, D.,Wang-Kan, X., Neuberger, A., van Veen, H.W., Pos, K.M., Piddock, L.J.V., Luisi, B.F. **2018** Multidrug efflux pumps: structure, function and regulation. *Nat Rev Microbiol.*, *16*, 523–539.

Henderson PJF, Maher C, Elbourne LDH, Eijkelkamp BA, Paulsen IT, Hassan KA 2021 Physiological functions of bacterial ‘multidrug’ efflux pumps. *Chem. Rev.* 2021, 121, 9, 5417–5478

Pasqua M, Bonaccorsi di Patti MC, Fanelli G, Utsumi R, Eguchi Y, Trirocco R,

Prosseda G, Grossi M, Colonna B. 2021. Host - Bacterial Pathogen Communication: The

Wily Role of the Multidrug Efflux Pumps of the MFS Family. Front Mol Biosci.

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Pasqua M,